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The relationship of passive smoking to various health outcomes among Seventh-day Adventists in California

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The Relationship of Passive Smoking to Various Health Outcomes among Seventh-day Adventists in California

A dissertation submitted in partial satisfaction

of the requirements for the degree

Doctor of Public Health

by

Terrence Leslie Butler

1988

The dissertation of Terrence Leslie Butler is approved.

Sander Greenland

William Shonick

Henry Gong

Murray Jarvik

Barbara Visscher, Committee Chair

University of California, Los Angeles

1988

Dedicated to the memory of my mother

Sarah Joan Butler (1922-1987)

A life of immeasurable qualities

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CHAPTER 5: LUNG CANCER RESULTS

In this chapter the results of the lung cancer analyses are presented for both the spouse pairs females and the AHSMOG cohort. For the spouse pairs females the initial analyses include both the current and past smokers. However, later analyses are restricted to the non-smoking population of this cohort. Although the major variables of interest are the passive smoking exposures, other selected factors are chosen for inclusion in the analyses because they may be independent risk factors or have some protective effect on the outcome. The methods of analyses included the calculation of a crude measure of effect and stratified analyses.

5.1 SPOUSE PAIRS COHORT

In the female population of the spouse pairs cohort nine incident cases of primary lung cancer were diagnosed during the follow-up period 1977 to 1982. Histological confirmation was obtained for each case and the information abstracted from medical pathology reports. The distribution by histological type is presented in Table 5.1. Since there were very few cases these were grouped together for analytical purposes and no effort was made to differentiate by various histological types.

TABLE 5.1

SPOUSE PAIRS - FEMALES
HISTOLOGY OF LUNG CANCER CASES

Histological Type	Number
Large cell carcinoma	1
Oat cell carcinoma	1
Adenocarcinoma	7

All the cases occurred in the age range of 45 to 69 and only one of the nine cases was diagnosed in a former smoker. No cases occurred among females classified as current smokers while eight cases were among non-smokers. Table 5.2 presents the distribution of incident cases, person years and incidence rates by ten year age groups according to the smoking status of subject and spouse.

A stratified analysis, stratifying on ten year age groups, was performed and Mantel-Haenszel summary rate ratios and corresponding 95% confidence intervals were calculated for selected exposure factors. The incidence rates, crude rate ratios, age adjusted rate ratios, confidence intervals and p-values are shown in Table 5.3. The differences between the crude rate ratios and adjusted rate ratios indicate that there was a

TABLE 5.2

SPOUSE PAIRS - FEMALES
LUNG CANCER (1977-1982)
DISTRIBUTION OF INCIDENT CASES, PERSON YEARS AND INCIDENCE RATES BY AGE GROUP AND HUSBAND SMOKING STATUS IN MARRIAGE

	WIFE NON SMOKER				WIFE SMOKER			
	HUSBAND SMOKER		HUSBAND NON SMOKER		HUSBAND SMOKER		HUSBAND NON SMOKER	
Age Group	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY
25-34	0 942	0.00	0 8004	0.00	0 718	0.00	0 836	0.00
35-44	0 1552	0.00	0 8637	0.00	0 899	0.00	0 816	0.00
45-54	1 2190	4.57	2 9520	2.10	0 1011	0.00	0 842	0.00
55-64	1 3000	3.33	2 8578	2.33	1 1240	8.06	0 875	0.00
65-74	1 2159	4.63	1 5980	1.87	0 829	0.00	0 305	0.00
75-84	0 682	0.00	0 2112	0.00	0 70	0.00	0 39	0.00
85-94	0 63	0.00	0 220	0.00	0 0	0.00	0 8	0.00
Total	3 10579	2.84	5 43052	1.16	1 4668	2.14	0 3619	0.00

confounding effect by age that to some extent was accounted for in the stratified analysis. The small number of cases and low statistical power militate against the possibility of achieving statistically significant results. It is also impossible to assess effect modification with so few cases.

For our major exposure factor of interest, husband smoking status in marriage, summary rate ratios of 1.94 (95% C.I. 0.46-8.24) and 2.47 (95% C.I. 0.29-21.18) were obtained for past and current exposure respectively when compared to the referent group of never exposed. A similar doubling of the risk was observed when the husband's smoking status was dichotomized into never and ever smoked, RR of 2.04 (95% C.I. 0.54-7.65). No increased risk of lung cancer was observed in this population for the subjects own smoking status. However, when smokers of more than ten pack years of cigarette smoking were compared to the referent group of non-smokers there was increased risk observed, RR of 2.22 (95% C.I. 0.28-17.74). The solitary case in the exposed category illustrates the equivocal nature of these results.

There is a suggestion of a decreased risk for those subjects who have attended college versus those with a high school education or less and an increased risk for subjects with blue collar working spouses compared

TABLE 5.3

SPOUSE PAIRS - FEMALES
AGE ADJUSTED RATE RATIOS (RR) OF LUNG CANCER (1977-1982)
FOR SELECTED EXPOSURE FACTORS

Factor	Levels	* Cases/ Person Years	* Rate/ 10^6 PY	Crude RR	Adjusted RR** (95% C.I.)	
Husband Smoking status in marriage	Never	6.47278	106	Ref.	Ref.	
	Past	3.11564	259	2.44	1.94 (0.46-8.24)	
	Current	1.3912	256	2.41	2.47 (0.29-21.18)	p = 0.53
Husband smoked in marriage	No	6.47278	106	Ref.	Ref.	
	Yes	4.15560	257	2.43	2.04 (0.54-7.65)	p = 0.27
Female smoking status	Never	8.54891	146	Ref.	Ref.	
	Past	1.7559	132	0.91	0.86 (0.11-6.92)	p = 0.84
	Current	0.884	0	0.00	0.00	
Female Smoked	Non-smoker	8.54891	146	Ref.	Ref.	
	Smoker	1.8443	118	0.81	0.80 (0.10-6.38)	p = 0.83
Pack years of smoking female	None	8.56772	141	Ref.	Ref.	
	0-10	0.3534	0	0.00	0.00	
	> 10	1.2827	354	2.51	2.22 (0.28-17.74)	p = 0.58
Education	High School	4.21036	190	Ref.	Ref.	
	College +	4.43253	116	0.61	0.75 (0.20-2.83)	p = 0.64
Live in rural area	Yes	3.30201	99	Ref.	Ref.	
	No	6.32490	154	1.55	1.59 (0.38-6.65)	p = 0.53

TABLE 5.3 continued

Factor	Levels	* Cases/ Person Years	+ Rate 10^6 PY	Crude RR	Adjusted RR= (95% C.I.)	
Spouse Occupation	White Collar	2 34665	68	Ref.	Ref.	
	Blue Collar	5 26120	230	3 96	4.15 (0.78-22.15)	p = 0 10
Fruit Index	11 + times week	4 26189	153	Ref.	Ref.	
	4-10 times week	4 23951	167	1 09	1.22 (0 31-4 90)	
	0-3 times week	1 12005	83	0 54	0.64 (0.07-5 83)	p = 0 87
Beta Carotene Index	High	4 22404	179	Ref.	Ref.	
	Medium	4 19882	201	1.12	1.23 (0 31-4 92)	
	Low	1:21317	47	0.26	0.31 (0 03-2 82)	p = 0 45

* Discrepancies in cases and person years are due to missing values in exposure factors

\+ Rate per 1 million person years

= Mantel Haenszel summary rate ratio (RR) - adjusted for age

Ref. Referent group

Total Subjects - 11,060
Lung Cancer Cases - 9
Total Person Years - 64,497

to subjects with white collar working spouses. However, both results are subject to bias because of the unknown classification of one of the cases and the missing number of person years.

Since there was only one case among the 1,475 females who had ever smoked, it was difficult to assess the influence of active smoking on the overall effect of ETS exposure. Therefore further stratified analyses were restricted to the 9,378 never smoking females. The results of these analyses are presented in Table 5.4. Somewhat similar results are observed as in the previous analysis and the same caveats concerning effect modification, bias and statistical significance apply. For the variable husband smoked in marriage, the age-adjusted rate ratio was 2.02 (95% C.I. 0.48-8.56).

An additional analysis using the conditional maximum likelihood estimator and an exact method for sparse data was performed and the results compared with the Mantel-Haenszel estimates in Table 5.5. These results have similar point estimates with the mid probability exact binomial confidence intervals being somewhat wider and more conservative.

TABLE 5.4

SPOUSE PAIRS - FEMALE NON-SMOKERS
AGE ADJUSTED RATE RATIOS (RR) FOR LUNG CANCER (1977-1982)
FOR SELECTED EXPOSURE FACTORS

Factor	Levels	* Cases/ Person Years	+ Rate/ 10^6 PY	Crude RR	Adjusted RR=	(95% C.I.)	
Husband Smoking	Never	6 43037	116	Ref.	Ref.		
status in	Past	2 8090	247	2 13	1 69	(0 32-8 88)	
marriage	Current	1 2486	402	3 47	3 37	(0 39-29 05)	p = 0 46
Husband smoked	No	6 43037	116	Ref.	Ref.		
in marriage	Yes	3 10575	284	2 45	2 02	(0 48-8 56)	p = 0 32
Education	High School	3 18063	187	Ref.	Ref.		
	College +	6 38670	129	0 69	0 86	(0 20-3 67)	p = 0 82
Live in rural	Yes	3 26013	115	Ref.	Ref.		
area	No	4 27694	144	1 26	1 30	(0 29-5 81)	p = 0 73
Spouse	White collar	2 31217	64	Ref.	Ref.		
Occupation	Blue collar	5 20768	289	4 51	4 89	(0 89-26 71)	p = 0 06
Beta Carotene	High	4 19454	206	Ref.	Ref.		
Index	Medium	3 17065	176	0 85	0 93	(0 21-4 17)	
	Low	1 17680	57	0 27	0 33	(0 04-2 99)	p = 0 59

* Discrepancies in cases and person years are due to missing values in exposure factors

\+ Rate per 1 million person years

= Mantel Haenszel summary rate ratio (RR) - adjusted for age

Ref Referent Group

Total Subjects - 9,378
Lung Cancer Cases - 8
Total Person Years - 54 898

TABLE 5.5

SPOUSE PAIRS - FEMALE NON-SMOKERS
A COMPARISON OF LUNG CANCER AGE ADJUSTED RATE RATIOS
FOR EXPOSURE TO SPOUSE SMOKING USING
DIFFERENT STATISTICAL METHODS

FACTOR	LEVELS	•	METHOD	ADJUSTED RR (95% C.I.)
Husband smoked in Marriage	No	9/43007	Mantel-Haenszel	Ref.
	Yes	3/10575		2.02 (0.49-8.56)
	No		Maximum Likelihood	Ref.
	Yes			2.01 (0.39-8.79)*

• cases/person years
* mid probability (Miettinen) binomial confidence intervals

5.2 AHSMOG COHORT

During the years 1977-1982 thirteen incident cases of lung cancer were diagnosed in the current non-smokers of the AHSMOG cohort. Seven of the cases were males and six were females. The histological types of tumors are presented in Table 5.6. As with the spouse pairs cohort the most predominant histological type was adenocarcinoma. However, all histological types were grouped together for analytical purposes.

TABLE 5.6

AHSMOG
HISTOLOGY OF LUNG CANCER CASES

Histological Type	Male	Female
Large cell carcinoma	1	
Carcinoma NOS	1	1
Squamous cell carcinoma	1	
Adenocarcinoma	4	4
Unknown		1

For females, cases occurred in the age range of 55 to 94 years while for males, cases were limited to the 55-84 year age range. The distribution of incident cases, person years and incidence rates by ten year age groups for the two ETS exposures of interest—years lived with a smoker and years worked with a smoker—are presented in Tables 5.7 and 5.8 respectively. There is an increased risk for age, however, the lack of sufficient cases prevent a careful assessment of trend across passive smoking exposures.

TABLE 5.7

AUSMOD - CURRENT NON SMOKERS
LUNG CANCER (1977-1982)
DISTRIBUTION OF INCIDENT CASES, PERSON YEARS AND INCIDENCE RATES BY AGE GROUP AND YEARS LIVED WITH A SMOKER

	YEARS LIVED WITH SMOKER					
	NONE		1-10 YEARS		11 + YEARS	
FEMALE Age Group	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY
25-34	0 636	0 00	0 243	0 00	0 386	0 00
35-44	0 1671	0 00	0 420	0 00	0 1149	0 00
45-54	0 2617	0 00	0 847	0 00	0 1628	0 00
55-64	0 3298	0 00	0 872	0 00	1 2269	4.41
65-74	1 2687	3 72	0 677	0 00	1 1791	5 58
75-84	1 1399	7.15	0 254	0 00	0 789	0 00
85-94	1 340	29 41	0 69	0 00	1 159	62 89
Total	3 12647	2.37	0 3292	0 00	3 8171	3 67
MALE Age Group						
25-34	0 382	0 00	0 103	0 00	0 142	0 00
35-44	0 980	0 00	0 268	0 00	0 379	0 00
45-54	0 2109	0 00	0 495	0 00	0 779	0 00
55-64	2 2371	8 44	0 483	0 00	0 995	0 00
65-74	0 1683	0 00	0 311	0 00	2 596	33 58
75-84	3 878	34 17	0 61	0 00	0 204	0 00
85-94	0 212	0 00	0 6	0 00	0 11	0 00
Total	6 8616	6 80	0 1728	0 00	2 3107	6 44

TABLE 5.8

AHSMOG - CURRENT NON SMOKERS
LUNG CANCER (1977-1982)
DISTRIBUTION OF INCIDENT CASES, PERSON YEARS AND INCIDENCE RATES BY AGE GROUP AND YEARS WORKED WITH A SMOKER

	YEARS WORKED WITH SMOKER					
	NONE		1-10 YEARS		11 + YEARS	
FEMALE Age Group	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY	Cases/ Person years	Rate/ 10,000 PY
25-34	0 621	0 00	0 588	0 00	0 155	0 00
35-44	0 1463	0 00	0 1195	0 00	0 583	0 00
45-54	0 2355	0 00	0 1640	0 00	0 1197	0 00
55-64	0 3532	0 00	1 1397	7.16	0 1610	0 00
65-74	1 3379	2 96	0 768	0 00	1 919	10 88
75-84	1 1953	5 12	0 255	0 00	0 234	0 00
85-94	2 439	45.68	0 72	0 00	0 59	0 00
Total	4 13641	2.93	1 6802	1.72	1 4657	2.16
MALE Age Group						
25-34	0 313	0 00	0 238	0 00	0 75	0 00
35-44	0 760	0 00	0 595	0 00	0 272	0 00
45-54	0 1797	0 00	0 936	0 00	0 650	0 00
55-64	2 2242	8 92	0 822	0 00	0 785	0 00
65-74	2 1718	11 64	0 440	0 00	0 432	0 00
75-84	1 860	11 63	2 98	204 08	0 186	0 00
85-94	0 193	0 00	0 30	0 00	0 7	0 00
Total	5 7883	6 34	2 3160	6 33	0 2408	0 00

There were no cases of lung cancer for either sex in the subjects who had lived for 1-10 years with a smoker. For males there were no cases among those who had worked eleven years or more with a smoker.

Four of the thirteen cases occurred among former smokers all of whom smoked more than ten pack years of cigarettes. In a stratified analysis, adjusting for age and sex, the rate ratio of lung cancer among those smoking more than ten pack years compared to those who were non-smokers was 2.81 (95% C.I. 0.78-10.20, p = 0.08). Consequently, past active smoking exposure was treated as a confounder and controlled for by stratification in additional analyses.

The results of stratified analyses for selected exposure factors controlling for age and subjects past smoking status are presented in Table 5.9 for females and Table 5.10 for males. The differences in the crude RR and adjusted RR indicate some confounding due to past active smoking and/or age differences in the population and therefore the adjusted summary rate ratios are considered as unconfounded by the subjects past smoking status or age. For females who had lived eleven or more years with a smoker as compared to females who had never lived with a smoker the rate ratio of lung cancer was 1.16 (95% C.I. 0.20-6.61). For females who had worked eleven or more years with a smoker the corresponding rate ratio was 1.47 (95% C.I. 0.15-14.06).

TABLE 5.9

AHSMOG - FEMALES
ADJUSTED RATE RATIOS (RR) OF LUNG CANCER (1977-1982)
FOR SELECTED EXPOSURE FACTORS

Factor	Levels	* Cases/ Person Years	+ Rate/ 10^6 PY	Crude RR	Adjusted RR~ (95% CI)		
Years Lived	None	3 12818	234	Ref.	Ref.		
with Smoker	1-10 years	0 3301	0	0 00	0 00		
	11 + years	3 8213	365	1.66	1.18	(0 20-6 61)	p = 0 68
Years Worked	None	4 13861	289	Ref.	Ref.		
with Smoker	1-10 years	1 5802	172	0 60	1.03	(0 11-10 11)	
	11 + years	1 4670	214	0 74	1.47	(0.15-14 06)	p = 0 99
Hours of	0-160	1 6273	159	Ref.	Ref.		
Oxidant	161-3000	4 13424	298	1 87	1.73	(0 20-16 25)	
> 10 ppm	> 3000	1 4635	216	1.36	0 90	(0 05-14 93)	p = 0 80
Hours of	0 100	1 5328	188	Ref.	Ref.		
TSP	101-3000	4 13039	307	1 63	1 25	(0 14-11 20)	
> 200 ppm	> 3000	1 5966	168	0 89	0 59	(0 04-9 81)	p = 0 83
Education	High School	3 9213	326	Ref.	Ref.		
	College +	3 14968	200	0 61	1 22	(0 24-6 22)	p = 0 82
Beta Carotene	High	2 8590	233	Ref.	Ref.		
Index	Medium	3 7197	417	1 79	1 81	(0 30-10 85)	
	Low	1 8228	121	0 52	0 35	(0 03-4 19)	p = 0 41

* Discrepancies in cases and person years are due to missing values in exposure factors

\+ Rate per 1 million person years

~ Mantel Haenszel summary rate ratio (RR) adj for age & smoking status

Total Subjects - 4,024
Cancer Cases - 6
Total Person Years - 24,100

TABLE 5.10

AUSMOD - MALES
ADJUSTED RATE RATIOS (RR) OF LUNG CANCER (1977-1982)
FOR SELECTED EXPOSURE FACTORS

Factor	Levels	* Cases/ Person Years	+ Rate/ 10^6 PY	Crude RR	Adjusted RR~ (95% C.I.)	
Years Lived	None	5 8723	573	Ref.	Ref.	
with Smoker	1-10 years	0 1729	0	0 00	0 00	
	11 + years	2 3123	640	1.12	1.17	(0 21-6.61) p = 0 84
Years Worked	None	5 7996	625	Ref.	Ref.	
with Smoker	1-10 years	2 3159	633	1 01	1.72	(0 33-9.04) p = 0.35
	11 + years	0 2420	0	0 00	0 00	
Hours of	0-160	0 3504				
Oxidant	161-3000	4 7429				
> 10 ppm	> 3000	3 2642				
Hours of	0-100	0 3084				
TSP	101-3000	3 6894				
> 200 ppm	> 3000	4 3618				
Education	High School	3 3821	785	Ref.	Ref.	
	College +	3 9692	310	0 39	0 66	(0 17-3 77) p = 0 62
Beta Carotene	High	1 4114	243	Ref.	Ref.	
Index	Medium	3 4019	746	3 07	4 01	(0 41-39 46)
	Low	2 5302	377	1 55	1 98	(0 18-21.73) p = 0 23

* Discrepancies in cases and person years are due to missing values in exposure factors

\+ Rate per 1 million person years

~ Mantel Haenszel summary rate ratio (RR) adj for age & smoking status

Total Subjects - 2,261
Cancer Cases - 7
Total Person Years - 13,455

Similar results are observed in Table 5.10 for the male cohort. There is a slight increased risk for subjects who lived eleven or more years with a smoker as compared to those who had not lived with a smoker, RR = 1.17 (0.21-6.61). For ETS exposure at work the rate ratio of lung cancer in males is 1.72 (95% C.I. 0.33-9.04). Since we have very few cases the conditional maximum likelihood RR estimate and the exact mid probability binomial confidence intervals were also calculated and the results are detailed in Table 5.11. These results are similar to the Mantel-Haenszel stratified analysis.

5.3 SUMMARY

In both populations analyzed there appears to be a positive effect of passive smoking exposure with the outcome of lung cancer. Each of the adjusted measures of effect for all the ETS variables show a positive effect for exposure. However, the magnitude of that effect varies depending on the cohort observed and the particular exposure variable used. For both sexes in the AHSMOG cohort the results indicate that working with a smoker has a greater effect on lung cancer than living with a smoker. However, the results should be interpreted cautiously because of the small number of cases that occurred in both populations. Further discussion of the results are presented in the final chapter.

TABLE 6.11

AHSMOG - LUNG CANCER
* ADJUSTED RATE RATIOS FOR VARYING YEARS
AND TYPES OF PASSIVE SMOKING EXPOSURE

Passive Smoke Exposure	Females Cases/PY	RR (95% CI)**		Males Cases/PY	RR (95% CI)**	
Years Lived with Smoker						
None	3/12818	Ref.		5/8723	Ref.	
1-10	0/3301	0.00		0/1729	0.00	
11 +	3/8213	1.22	(0.18-7.89)	2/3123	1.18	(0.15-6.74)
			p = 0.82			p = 0.83
Years Worked with Smoker						
None	4/13861	Ref.		5/7996	Ref.	
1-10	1/5802	1.01	(0.04-9.09)	2/3159	1.68	(0.22-8.81)
11 +	1/4570	1.38	(0.05-12.56)	0/2420	0.00	
			p = 0.76			p = 0.55

* Conditional maximum likelihood estimates of RR adjusted for age and past smoking status

** Mid probability (Miettinen) binomial confidence interval